Department of Forensic Science

TOXICOLOGY TRAINING MANUAL

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1 INTRODUCTION

1.1 Purpose and Scope

1.1.1 The purpose of this manual is to define the training program for forensic lab specialists, forensic scientists and toxicologists working in the toxicology section as employees of the Commonwealth of Virginia Department of Forensic Science. This work is intended to be used in a formal training program that will establish a certain minimum standard of professional competency throughout the toxicology section statewide.

1.1.2 The manual is organized in modules and each module outlines the objectives, time expected to complete training in a specific topic, methods of instruction, modes of evaluation and study questions.

1.1.3 The training program covers theory and methodology of instrumentation, analytical techniques, interpretation of analytical results, report writing, data and case review, and handling of evidence.

1.1.4 The training program provides exposure to court room testimony and legal aspects throughout the training and assists in developing the skills necessary to be an effective expert witness.

1.1.5 The program evaluates the progress and performance of the trainee with each module. Each module includes laboratory exercises, competency tests and study questions. Upon completion of each module, the trainee with give an oral presentation on the module material which will be followed by a question/answer session to ensure the trainee understands the module material.

1.1.6 The sequence in which the modules are presented should not necessarily be considered as a mandatory order of instruction.

1.1.7 The trainee will complete a mini-technical final after the first 6 modules and a second mini-technical final on the remaining modules.

1.1.8 It is recognized that some of the forensic laboratory specialists may only perform certain analyses. Therefore, FLS III and VI's are only required to complete the modules associated with the type of work they perform, not necessarily the entire training manual (e.g., FLS III who performs immunoassay screening must complete laboratory exercises, competency tests, study questions and oral presentation in the Immunoassay Module).

1.1.9 Forensic scientists are expected to complete Modules 1-12 and 15.

1.1.10 Forensic toxicologists are expected to complete Modules 1-12 and 14-15. Upon completion of module 14, the toxicologist's knowledge in pharmacology and toxicology will be assessed in a pharmacology technical oral examination.

1.1.11 Any member of the toxicology section who performs examinations of alcoholic beverages will be required to complete Module 13 (Alcoholic Beverage Analysis). Since alcoholic beverage analyses are only conducted in the Central Laboratory by select personnel, most Trainees will not complete this section.

1.1.12 The program culminates in the final competency exercise which includes a practical test, an analytical technical oral examination and a moot court.

1.2 Coordination of the Program

1.2.1 The training coordinator is usually the supervisor (toxicologist) in each laboratory.

1.2.2 The coordinator will be responsible for the overall training, but may delegate certain duties and blocks of instruction to other individuals.

1.3 Training Period

1.3.1 The length of the training period is a highly variable matter and will be left to the determination of the Chemistry Program Manager. Certain individuals may require less time than others, depending on experience, education or learning ability. However, the training period is usually completed within 12 months.

1.4 Location of Training

1.4.1 Whenever practical, the bulk of an individual's training will occur in the laboratory to which they will be assigned. Toxicologists are typically trained in the Central Toxicology Laboratory unless there is another toxicologist present in the regional lab to provide training.

1.5 Training Goals

1.5.1 The training should culminate such that the trainee has the following:

1.5.1.1 The knowledge of analytical chemistry.

1.5.1.2 The knowledge of the principles and practices of forensic toxicology related to the analysis of drugs and poisons within biological samples.

1.5.1.3 The knowledge of the theory and application of a variety of instruments used for the identification and quantitation of drugs.

1.5.1.4 The ability to perform accurate forensic toxicology analyses independently and proficiently.

1.5.1.5 The ability to skillfully present and defend analytical findings in courts of law.

1.6 Instructions to the Trainee

1.6.1 The trainee is expected to document all their training activity and to provide a weekly progress report to the training coordinator. The progress report should also include upcoming training goals.

1.6.2 Once the trainee has demonstrated his/her competence to perform a particular analysis through the completion of specific training module(s), the trainee may authorized by the Chemistry Program Manager on recommendation by the Section Supervisor to perform those analyses on case work. This authorization will be documented via MFR. Batch data run by trainees must be reviewed by a qualified examiner/FLS VI and this review be documented on the batch summary worksheet. Trainees may not act as batch reviewers.

1.7 Instructions to Training Coordinators

1.7.1 As previously stated, the intent of the training manual is to define a program that will ensure each and every trainee receives certain basic principles and fundamentals necessary to the complete education of lab specialists, forensic scientists or toxicologists within the toxicology section. All of the listed topics must be incorporated into the program for forensic scientists and toxicologists. However, it is recognized that some of the forensic laboratory specialists may only perform certain analyses. Therefore, they are only required to complete the modules associated with the type of work they perform, not necessarily all the modules throughout the training program.

1.7.2 The training coordinator is responsible for maintaining the Department's training program documentation during the training period. Each section of the training log must be dated and initialed upon completion of the specified task. If any task is not completed, for any reason, this must be explained in the training file and approved by the Chemistry Program Manager.

1.7.3 Once the trainee has satisfactorily completed all of the requirements of the program, the Chemistry Program Manager shall forward a written recommendation for certification to the Department Director.

1.7.4 If the trainee cannot meet the criteria expected of them during the training period, steps must be taken to effect appropriate action.

1.7.5 The performance of the trainee will be evaluated during the course of the program. The TC must submit regular written evaluations of the new chemist's progress to the Chemistry Program Manager. The coordinator is to discuss this evaluation with the trainee prior to forwarding it to the Chemistry Program Manager. Any relevant comments by either the trainee or coordinator are to be included with the report. The report should also be forwarded to the laboratory director.

1.7.5.1 The report should include both previous accomplishments and future objectives.

1.7.5.2 A copy of the report will be placed in the training file.

1.8 Moot Court

1.8.1 The training coordinator is responsible for ensuring that the trainee is thoroughly prepared for legal questioning. This can be done by a combination of moot courts, prearranged as well as impromptu question and answer sessions, and observation of courtroom testimony given by experienced examiners.

1.8.2 The scheduling of practice moot courts is to be done by the training coordinator. These are to be conducted throughout the training period.

1.9 Guidelines for Technical Examinations, Practical Test, and Final Moot Court

1.9.1 Final Analytical Technical Examination

1.9.1.1 Prior to the final moot court, a technical oral examination of the trainee will be conducted to ascertain the analytical knowledge of the individual. This will be limited to 3 hours.

1.9.1.2 After the examination, supervision/management will discuss the trainee’s performance.

1.9.1.3 The outcome of the examination will be satisfactory or not satisfactory.

1.9.1.4 If the panel determines that the trainee’s performance was not satisfactory, steps must be taken to effect the appropriate action.

1.9.2 Pharmacology Technical Examination (Toxicologists only)

1.9.2.1 Prior to the final moot court, a pharmacology technical oral examination of the toxicologist trainee will be conducted to ascertain their knowledge of pharmacology, toxicology and interpretation of results. This will be limited to 3 hours.

1.9.2.2 After the examination, supervision/management will discuss the trainee’s performance.

1.9.2.3 The outcome of the examination will be satisfactory or not satisfactory.

1.9.2.4 If the panel determines that the trainee’s performance was not satisfactory, steps must be taken to effect the appropriate action.

1.9.3 Practical examination

1.9.3.1 Following successful completion of all training modules, the trainee will be given a practical test to work as though it were a real case.

1.9.3.2 The practical test will be a typical case involving at least 3 analytical procedures (e.g., alcohol screen, immunoassay screen and confirmation/quantitation).

1.9.3.3 The trainee will generate an associated case file and Certificate of Analysis for the practical test.

1.9.4 Moot court

1.9.4.1 A taped final moot court will be conducted regarding the analysis of the practical test.

1.9.4.2 The Chemistry Program Manager must agree with the selection of all participants.

1.9.4.3 The atmosphere will be formal, that is, it will be conducted in the same manner as a real courtroom situation. This includes dress, conduct, protocol and all other aspects. Answers and explanations are to be directed as to a lay jury or judge.

1.9.4.4 The moot court will not exceed 2 hours.

1.9.4.5 The role of the prosecutor will be assumed by the training coordinator or designee.

1.9.4.6 The moot court may be stopped at any time upon request of any of the involved parties.

1.9.4.7 After the court, supervision/management will assess the trainee's performance.

1.9.4.8 The outcome of the moot court will be satisfactory or not satisfactory.

1.9.4.9 If the panel determines that the trainee's performance was not satisfactory, steps must be taken to effect the appropriate action.

1.9.4.10 This evaluation will be immediately followed by a short performance critique.

1.9.4.11 The training coordinator will review the video tape of the trial with the trainee as soon as possible. Other participants/observers should provide comments to the training coordinator as soon as possible.

1.10 Transition from Trainee to Examiner

1.10.1 After the new examiner has successfully completed this training, there follows a period of adjustment. The job of the coordinator is to ensure that this transition from training to real life takes place as smoothly as possible.

1.10.2 Casework will be introduced stepwise under the close supervision of a senior examiner.

1.10.3 The supervisor, training coordinator or designee will accompany and monitor the newly qualified examiner to court for the first few cases.

1.11 Continuing Education

1.11.1 All forensic lab specialists, forensic scientists and toxicologists should participate in continuing education to maintain their skills and state of the art knowledge in the field of forensic toxicology.

1.11.2 Examples of continuing education include:

- Attendance at meetings, workshops or seminars
- Participation in study groups or scientific working groups
- Review of current literature

- Publication or presentation of research or case reports
- Education/training/teaching in the field of forensic toxicology
- Participation in specialized courses

2 ORIENTATION

2.1 Minimum Requirements for Orientation

2.1.1 Introduction to local operating facilities and personnel.

2.1.2 Assignment of a work area.

2.1.3 Coverage of the following:

2.1.3.1 Quality Manual

2.1.3.2 Administrative Policies

2.1.3.3 Regional Operating Procedures

2.1.3.4 Toxicology Procedures Manual

2.1.3.5 DFS Safety Manual

2.1.3.6 Organization of the Department of Forensic Science

2.1.4 Introduction to the technical capabilities of all regional laboratories.

2.1.5 Explanation of the purpose of the training program including an insight into the course of events and what the trainee is expected to accomplish.

2.1.6 Explanation of the operation of local, state and federal law enforcement agencies and court systems.

2.1.7 Clarification of the duties of forensic laboratory specialists, forensic scientists and toxicologists within the Section.

2.1.8 Introduction to the LIMS system.

3 EVIDENCE RECEIVING AND HANDLING

3.1 Objectives

3.1.1 Understand physical evidence handling procedures used by DFS as detailed in the Quality Manual.

3.1.2 Understand physical evidence handling procedures pertinent to the toxicology section.

3.1.3 Receive and process evidence for the Office of the Chief Medical Examiner (OCME), driving under the influence (DUI/DUID) and police cases.

3.2 Estimated Time

Eight weeks (as 1/4 days)

3.3 Methods of Instruction

3.3.1 Lectures

3.3.1.1 Receiving and processing evidence

3.3.1.2 Evidence security

3.3.1.3 Chain of custody

3.3.1.4 LIMS system

3.3.2 Required Reading

3.3.2.1 Department of Forensic Science Quality Manual

3.3.2.2 Toxicology Procedures Manual

3.3.2.3 Code of Virginia, §18.2-266

3.3.2.4 Code of Virginia, §§18.2-268.1, 18.2-268.5 - 18.2-268.7

3.3.3 Demonstration

3.3.3.1 Evidence receiving and processing will be observed from beginning to end and notes will be taken by the Trainee.

3.3.4 Laboratory Exercises

3.3.4.1 The Trainee will receive and process evidence for at least 20 ME samples.

3.3.4.2 The Trainee will receive and process at least 20 samples each of DUI/DUID and/or police cases.

3.3.4.3 Maintain a list of processed samples for the training file.

3.4 Evaluation

3.4.1 Completion of written study questions.

3.4.2 Oral presentation followed by technical question/answer session.

3.5 Study Questions

3.5.1 List all procedural steps involving evidence from receiving to final disposition for each of the following: DUI/DUID, ME and police cases.

3.5.2 Define the following terms: chain of custody, lock box, evidence seal, convenience packaging, RFLE, FS lab #, LIMS.

3.5.3 Define a proper seal.

3.5.4 Who has access to the main evidence storage room? Toxicology storage refrigerators?

3.5.5 Who has access to your work area?

3.5.6 What actions are taken to ensure the proper preservation of evidence?

3.5.7 Describe the disposition of evidence (ME, DUI, DUID, police) after results have been reported?

3.5.8 When is evidence returned to the originating agency?

3.5.9 List commonly encountered problems associated with receipt of evidence and subsequent actions taken.

3.5.10 What is the official chain-of-custody record for the following:

- Submission of a DUI/D case submitted with an RFLE
- Submission of a DUI/D case submitted without an RFLE
- Submission of an OCME case
- Placement of DUI/D samples into section storage
- Removal of item from section storage for analysis
- Return of item to section storage after analysis

4 BLOOD ALCOHOL ANALYSIS

4.1 Objectives

4.1.1 Understand the theory and application of headspace gas chromatography (GC).

4.1.2 Comprehend the function and the specifics of operation of headspace GC.

4.1.3 Prepare specimens for analysis by headspace GC.

4.1.4 Operate the headspace GC.

4.1.5 Calibrate the instrument and quantitate ethanol, methanol, acetone and 2-propanol.

4.1.6 Interpret results by thoroughly examining and explaining the chromatograms.

4.1.7 Understand the use of internal and external standards.

4.1.8 Demonstrate proficiency by analyzing two full runs (20 samples each) of blood alcohol cases.

4.1.9 Process results and record results of medical examiner, DUI/DUID and police casework.

4.1.10 Understand the uncertainty of measurement including how it is calculated and explained in court.

4.2 Estimated Time

One month

4.3 Methods of Instruction

4.3.1 Lectures

4.3.1.1 Principles of headspace GC

4.3.1.2 Operation of the headspace GC

4.3.1.3 Specimen preparation (dilution, internal standard, external standard)

4.3.1.4 Calibration and QC

4.3.1.5 Result interpretation

4.3.1.6 Paperwork processing in medical examiner, DUI/DUID and police casework

4.3.2 Required Reading

4.3.2.1 Garriott, J. C., *Medicolegal Aspects of Alcohol*. 4th[d] Ed. 2003, Lawyers & Judges Pub. Co, Inc.

4.3.2.2 Barry Levine (2003) *Principles of Forensic Toxicology*, pp 157-172

4.3.2.3 Toxicology Procedures Manual

4.3.2.4 Code of Virginia (§18.2-268)

4.3.2.5 Moffat, A.C., editor. *Clarke's Analysis of Drugs and Poisons*, 3rd edition. London: The Pharmaceutical Press, 2004 pp 53-67.

4.3.3 Demonstration

4.3.3.1 Blood alcohol analysis and operation of the headspace GC will be observed from beginning to end and notes will be taken by the Trainee.

4.3.4 Laboratory Exercises

4.3.4.1 Analyze one batch of 20 ME blood specimens for ethanol. At least 5 of the specimens will be positive for ethanol and at least one specimen will be negative.

4.3.4.2 Analyze one batch of 20 DUI blood specimens for ethanol. At least 10 of the specimens will be positive for ethanol and at least one specimen will be negative.

4.4 Evaluation

4.4.1 Completion of written study questions.

4.4.2 Laboratory Competency Testing

4.4.2.1 A series of at least 20 previously analyzed ME blood specimens will be presented to the Trainee for a routine blood alcohol analysis. Trainee's results must fall within the uncertainty of measurement of the previous results. Trainee's results must fall within ± 6% of the reported value.

4.4.2.2 A series of at least 20 previously analyzed DUI/DUID blood specimens will be presented to the Trainee for a routine blood alcohol analysis. Trainee's results must fall within the uncertainty of measurement of the previous results. Trainee's results must fall within ± 6% of the reported value.

4.4.3 Oral presentation followed by technical question/answer session

4.5 Study Questions

4.5.1 Explain the principle and operation of headspace gas chromatography.

4.5.2 Explain when calibration or recalibration of the headspace GC is necessary. How is recalibration accomplished?

4.5.3 What is NIST? Why is it important?

4.5.4 Discuss the relationship between the concentration of alcohol in blood with that in urine, serum, and vitreous humor.

4.5.5 Explain the difference between serum and blood ethanol.

4.5.6 Explain what causes the blood alcohol concentration in a specimen to either decrease or increase. What measures can be taken to prevent this?

4.5.7 Explain the ethanol interconversion between mg/L, mg/dL, µg/mL and gm%. Present 5 examples of each.

4.5.8 What is the purpose of running a mixed volatile control during the prerun?

4.5.9 Manually calculate BAC based on response of ethanol, internal standard and calibrators.

4.5.10 What are the properties of a good internal standard?

4.5.11 What is the UOM for the alcohol assay and what does it mean? How would you explain UOM in a courtroom?

5 IMMUNOASSAY

5.1 Objectives

5.1.1 Understand and explain immunoassay.

5.1.2 Understand the theory of commonly used immunoassay testing methods.

5.1.3 Understand the theory and practice of Immunalysis ELISA system.

5.1.4 Prepare tissue specimens for analysis by ELISA.

5.1.5 Perform Immunalysis ELISA screening

5.1.6 Interpret results by thoroughly explaining the calculations and instrument printouts

5.1.7 Understand the quality control aspects of ELISA screening.

5.2 Estimated Time

Four weeks (as ½ days)

5.3 Methods of Instruction

5.3.1 Lectures

5.3.1.1 Principles of immunoassay

5.3.1.2 Types of immunoassays

5.3.1.3 Components and operation of ELISA

5.3.1.4 Specimen preparation

5.3.1.5 Specimen analysis

5.3.1.6 Result interpretation

5.3.2 Required Reading

5.3.2.1 Barry Levine (2003) *Principles of Forensic Toxicology*, pp 117-137.

5.3.2.2 Moffat, A.C., editor. *Clarke's Analysis of Drugs and Poisons*, 3rd edition. London: The Pharmaceutical Press, 2004 pp 301-312.

5.3.2.3 TECAN® Miniprep Operator's Guide

5.3.2.4 Toxicology Procedures Manual

5.3.3 Demonstration

5.3.3.1 ELISA analyses will be observed from beginning to end and notes will be taken by the Trainee.

5.3.4 Laboratory Exercises

5.3.4.1 Analyze one batch of 10 blood specimens by ELISA screening for at least 10 different classes of drugs. At least 5 of the specimens will be above the cutoff concentration and at least one specimen below the cutoff.

5.4 Evaluation

5.4.1 Completion of written study questions.

5.4.2 Laboratory Competency Testing

5.4.2.1 Qualitative – a series of at least 10 previously analyzed blood specimens will be presented to the Trainee for a routine DUID panel according to the Toxicology Procedures Manual. Qualitative results obtained by the Trainee must agree with previous results.

5.4.3 Oral presentation followed by technical question/answer session

5.5 Study Questions

5.5.1 Explain the advantages and disadvantages of screening for the presence of drugs.

5.5.2 Describe the following three different types of immunoassay: radioimmunoassay (RIA), enzyme linked immunosorbent assay (ELISA), and fluorescence polarization immunoassay (FPIA).

5.5.3 Explain the following terms as they apply to ELISA: antigen, antibody, monoclonal/polyclonal antibody, microplate, substrate, horseradish peroxidase, cross-reactivity, cutoff, limit of detection, true-positive, false-positive, sensitivity, false negative and specificity.

5.5.4 Distinguish between homogeneous (e.g., enzyme multiplied immunoassay technique (EMIT)), and heterogeneous immunoassays (ELISA).

5.5.5 Explain cross-reactivity stating advantages and disadvantages. Include the significance of immunoassay specificity for a specific drug vs. the specificity for a drug class.

5.5.6 Name the chemical compound that is the primary target of the antibody in each of the ELISA assays.

5.5.7 Explain the relationship between absorbance and the concentration of the drug being determined.

5.5.8 Explain B/B0. How is it calculated?

5.5.9 Explain the role of the negative control, ½ cutoff, cutoff and positive control.

5.5.10 Describe the components of the ELISA kits and explain the purpose of each.

6 SPECTROPHOTOMETRY

6.1 Objectives

6.1.1 Understand and explain the principles of ultraviolet (UV), visible (VIS), and fluorescence spectrophotometric measurements.

6.1.2 Understand the practice of UV/VIS spectrophotometry and the specifics of operation of the spectrophotometers at DFS.

6.1.3 Perform instrumental analysis of carboxyhemoglobin using a UV/VIS spectrophotometer.

6.1.4 Interpret results by thoroughly examining and explaining the instrument printout.

6.1.5 Understand the quality control aspects of spectrophotometric testing.

6.2 Estimated Time

Two weeks

6.3 Methods of Instruction

6.3.1 Lectures

6.3.1.1 Principles of spectrophotometry and spectrofluorometry

6.3.1.2 Components and operation of the UV/VIS spectrophotometer

6.3.1.3 Specimen preparation

6.3.1.4 Specimen analysis

6.3.1.5 Result interpretation

6.3.1.6 Palladium chloride diffusion confirmation test

6.3.1.7 Salicylate confirmation by VIS spectrometry

6.3.2 Required Reading

6.3.2.1 Barry Levine (2003) *Principles of Forensic Toxicology*, pp 79-88.

6.3.2.2 Moffat, A.C., editor. *Clarke's Analysis of Drugs and Poisons*, 3rd edition. London: The Pharmaceutical Press, 2004 pp 313-327.

6.3.2.3 Toxicology Procedures Manual

6.3.3 Demonstration

6.3.3.1 The use of UV/VIS spectrophotometry for the quantitative analyses of carbon monoxide will be observed from beginning to end and notes will be taken by the Trainee.

6.3.4 Laboratory Exercises

6.3.4.1 Analyze low, medium and high controls for the presence of carbon monoxide (CO).

6.3.4.2 Screen one batch of 5 blood specimens for the presence of CO. At least 2 of the specimens will be positive and at least one specimen will be negative.

6.3.4.2.1 Calculate the % saturation of each specimen.

6.3.4.3 Confirm the presence of CO using the palladium chloride diffusion test.

6.4 Evaluation

6.4.1 Completion of written study questions.

6.4.2 Laboratory Competency Testing

6.4.2.1 A series of at least 5 previously analyzed blood specimens will be presented to the Trainee for CO analysis. The results obtained by the Trainee must agree within ±20% of the reported value.

6.4.3 Oral presentation followed by technical question/answer session.

6.5 Study Questions

6.5.1 What are the wavelength ranges for visible and ultraviolet electromagnetic radiation?

6.5.2 Explain what effects a change in solvent might have on the spectrum of a solute.

6.5.3 Discuss why a change in the pH of a solution can be important when using UV for analysis.

6.5.4 List and discuss some common sources of error in spectrophotometric measurements.

6.5.5 Define the following terms: wavelength, absorbance, transmittance, excitation, emission, bandwidth and Beer's law.

6.5.6 In the quantitative carboxyhemoglobin analysis, explain deoxyhemoglobin, oxyhemoglobin, methemoglobin and carboxyhemoglobin.

6.5.7 How are the results reported on the certificate of analysis for CO?

6.5.8 Explain the principle of the palladium chloride confirmation.

7 QUALITATIVE DRUG SCREENS

7.1 Objectives

7.1.1 Understand the theoretical and practical aspects of extractions.

7.1.2 Become familiar with various types of extractions.

7.1.3 Understand the theory of gas chromatography (GC) and mass spectrometry (MS).

7.1.4 Become familiar with the practical aspects of GC and MS.

7.1.5 Study the components of a gas chromatograph, and understand their function and specifics of operation.

7.1.6 Study the components of a GC/MS, and understand their function and specifics of operation.

7.1.7 Extract representative compounds (basic, acidic & neutral) from various matrices.

7.1.8 Perform qualitative drug identification of biological specimen extractions using NPD gas chromatography.

7.1.9 Perform qualitative drug identification of biological specimen extractions using full scan gas chromatography/mass spectrometry.

7.1.10 Examine and interpret gas chromatographic printouts.

7.1.11 Examine and interpret GCMS results by explaining and comparing the mass spectra to libraries and databases.

7.2 Estimated Time

Three months

7.3 Methods of Instruction

7.3.1 Lecture

7.3.1.1 Principles of extraction

7.3.1.2 Henderson-Hasselbach equation, acid base equilibrium

7.3.1.3 Buffers and ionization

7.3.1.4 Extraction

7.3.1.5 Liquid-liquid extraction

7.3.1.6 Solid phase extraction (SPE)

7.3.1.7 Principles of gas chromatography

7.3.1.8 Components and operation of GC

7.3.1.9 Parameters affecting the separation process and resolution of peaks

7.3.1.10 Types of injectors and injection techniques

7.3.1.11 Types of columns

7.3.1.12 Types of detectors

7.3.1.13 GC optimization

7.3.1.14 Principles of mass spectrometry: ionization, source, detection

7.3.1.15 MS components (sample inlets, ion sources, mass filters, detectors, vacuum systems)

7.3.1.16 Acquiring and evaluating mass spectra

7.3.1.17 Operation of GCMS in full scan mode

7.3.1.18 Use of libraries and databases

7.3.1.19 Specimen preparation (dilution, internal standard)

7.3.2 Required Reading

7.3.2.1 Solid Phase Extraction Techniques (United Chemical Technologies).

7.3.2.2 Toxicology Procedures Manual.

7.3.2.3 Moffat, A.C., editor. *Clarke's Analysis of Drugs and Poisons*, 3rd edition. London: The Pharmaceutical Press, 2004 pp 80-108, pp 379-391, pp 425-499.

7.3.2.4 Willard, H.H., Merritt, L.L. Jr., Dean , J., Settle, F.A., *Instrumental Methods of Analysis*, 7th Ed. 1988, Wadsworth Pub Co., pp 540-578.

7.3.2.5 Barry Levine (2003) *Principles of Forensic Toxicology*, pp 67-78, 89-116, 139-153.

7.3.2.6 *Forensic Applications of Mass Spectrometry* in Saferstein's *Forensic Science Handbook*. Englewood Cliffs, NJ: Prentice Hall, 1982 pp 117-159.

7.3.2.7 Pierce Catalog (Pierce Endogen) 2001-2002, *GC Derivatization and Labware*, Pages 497 – 526.

7.3.2.8 Comparison of Liquid/Liquid and Solid Phase Extraction for Alkaline Drugs, Juhascik, M. and Jenkins, A., Journal of Chromatographic Science, Vol 47, August 2009, p. 553-557.

7.3.3 References

7.3.3.1 Hyver, KJ. et al, *High Resolution Gas Chromatography*, 3rd Ed. 1989, Hewlett-Packard Co.

7.3.3.2 Rood, D. *A Practical Guide to the Care, Maintenance, and Troubleshooting of Capillary Gas Chromatography Systems*, 3rd Revised Ed. 1999, Wiley-VCH.

7.3.3.3 Mills, T and Robinson JC. *Instrumental Data for Drug Analysis*, 2nd Edition. Volumes 1-7, New York: Elsevier, 1987.

7.3.3.4 Watson, J. T. *Introduction to Mass Spectrometry*. 3rd Ed. 1997. Lipincott-Raven.

7.3.3.5 *Handbook of Analytical Derivatization Reactions*, Daniel R. Knapp, John Wiley, New York, 1979.

7.3.3.6 Agilent Technologies GCMS Instrument Manuals

7.3.4 Demonstration

7.3.4.1 The following extraction techniques will be observed from beginning to end and notes will be taken by the Trainee: Liquid-liquid extraction, solid phase extraction and drug identification by GC/NPD and GC/MS.

7.3.5 Laboratory exercises

7.3.5.1 Perform a liquid/liquid extraction of base screen drug mixes and 5 previously analyzed blood specimens for analysis by GC/NPD and GC/MS.

7.3.5.2 Perform a SPE extraction of base screen drug mixes and 5 previously analyzed blood specimens for analysis by GC/NPD and GC/MS.

7.3.5.3 Perform a liquid/liquid extraction of acid/neutral mixes and 3 previously analyzed blood specimens for analysis by GC/MS.

7.3.5.4 Determine the retention time and relative retention time (using the GC/NPD and methapyrilene as the internal standard) of basic drug mixes.

7.3.5.5 Use GC/MS and mass spectral libraries to identify drugs and metabolites in 50 drug screens (50 total of base and acid/neutral). Review all cases with a qualified forensic scientist/toxicologist to ensure all drugs and metabolites were correctly identified.

7.4 Evaluation

7.4.1 Completion of written study questions.

7.4.2 Laboratory Competency Testing

7.4.2.1 Liquid-liquid extraction - a series of 5 previously analyzed blood specimens will be presented to the Trainee for base extraction, screens and confirmation by GC/NPD and GC/MS. Qualitative findings must agree with previously reported results.

7.4.2.2 Solid phase extraction - a series of 5 previously analyzed blood specimens will be presented to the Trainee for for base extraction, screens and confirmation by GC/NPD and GC/MS. Qualitative findings must agree with previously reported results.

7.4.2.3 Liquid-liquid extraction - a series of 3 previously analyzed blood specimens will be presented to the Trainee for acid/neutral extraction, screens and confirmation by GC/MS. Qualitative findings must agree with previously reported results.

7.4.3 Oral presentation followed by technical question/answer session.

7.5 Study Questions

7.5.1 Describe liquid-liquid and solid-phase extractions stating the advantages and disadvantages of each type.

7.5.2 List and describe chemical forces which drive the movement of solute between aqueous and organic phases.

7.5.3 Explain the effects of pH on extractions.

7.5.4 List at least three different types of SPE sorbents, and how they interact with the substances being extracted.

7.5.5 List and explain the typical steps in an SPE procedure.

7.5.6 Define the following terms: matrix; functional group; polarity; solvents; pH; pKa; Henderson-Hasselbach equation; basic, acidic, neutral and amphoteric molecules; conjugate acid, conjugate base; internal standard; external standard.

7.5.7 What is gas chromatography?

7.5.8 What types of information are obtained from GC?

7.5.9 Draw a schematic diagram of a gas chromatograph and describe the function of each component.

7.5.10 What are the advantages of using relative retention time for drug identification rather than retention time?

7.5.11 Describe the different types of stationary phases used in the Toxicology Section.

7.5.12 List three different modes of sample introduction and state the advantages and disadvantages of each.

7.5.13 What factors govern the amount of sample to be injected? How much sample can the average capillary column hold? What factors influence this?

7.5.14 What temperature should the injection port be under normal circumstances and why?

7.5.15 What type of septum is recommended for GC work and why?

7.5.16 What is an injection port liner? What is it made of? Why is it used? Describe the packing process including the materials used.

7.5.17 What is a split ratio? How is it calculated?

7.5.18 Describe capillary and wide bore GC columns and state applications and limitations of each.

7.5.19 Describe the various GC detectors used in the toxicology section (i.e., FID, NPD, ECD) stating the application and limitation of each.

7.5.20 Describe the advantages and disadvantages of isothermal vs temperature programming.

7.5.21 Why is it necessary to regulate the carrier gas flow?

7.5.21.1 How is this done?

7.5.21.2 What factors influence the optimum flow rate for a given carrier gas?

7.5.21.3 If the carrier gas is too fast or too slow, how will it affect the peak shapes?

7.5.21.4 How will it affect the detector?

7.5.22 What is “make-up” gas? How and why is it used?

7.5.23 Explain the following statement: *response is proportional to the number of carbon atoms in the sample.* What type(s) of detector is this statement applicable to?

7.5.24 Discuss the operation of an autosampler.

7.5.25 What are the possible causes and remedies for the following GC problems?

7.5.25.1 No peaks

7.5.25.2 Tailing peaks

7.5.25.3 Leading peaks

7.5.25.4 Split peaks

7.5.25.5 Baseline drift

7.5.26 What is column bleed?

7.5.27 What is the effect of column bleed and/or septum bleed on GC/MS operation? What corrective action steps are normally taken?

7.5.28 When and why are columns conditioned? Describe the process.

7.5.29 Define the following terms:

- Carrier gas
- Height equivalent theoretical plate
- Mobile phase
- Resolution
- Stationary phase
- Partition coefficient
- Retention time
- Theoretical plates
- Column efficiency
- Make-up gas
- Van Deemter plot
- Phase ratio
- Selectivity
- Flow rate
- Relative retention time
- Signal to noise ratio

7.5.30 Describe the use of drug reference materials in the identification process.

7.5.31 What is mass spectrometry?

7.5.32 Draw a schematic diagram for a GC/MS and describe the function of each component.

7.5.33 Describe how a quadrupole mass filter operates.

7.5.34 Diagram and explain the functions of the components of the Agilent 5973/5975 EI source.

7.5.34.1 Are the ions formed positive or negative?

7.5.34.2 Do they have an even or odd number of electrons?

7.5.34.3 What is the ionization efficiency of this technique?

7.5.35 What vacuum conditions are necessary in the ionization source and the analyzing regions of a MS and why?

7.5.35.1 Describe how a rough pump works.

7.5.35.2 Describe how a diffusion pump works.

7.5.35.3 Describe how a turbomolecular pump works.

7.5.36 Briefly explain how chemical ionization is performed.

7.5.36.1 What are its advantages/disadvantages with respect to electron ionization?

7.5.36.2 What is the number of fragment ions produced by this method dependent on?

7.5.36.3 Do the ions formed by this process have an even or odd number of electrons?

7.5.37 Describe the difference between full mass scans and selective ion monitoring.

7.5.38 Describe the importance of autotuning and explain the Autotune report.

7.5.39 Explain the following MS terms:

- mass to charge ratio
- molecular ion
- parent ion
- base peak
- total ion chromatogram
- SIM
- mass resolution
- relative abundance
- scan rate
- spectral tilting

7.5.40 What is an extracted ion profile? How would you use it in drug identification?

7.5.41 How does the probability-based-matching library search work?

7.5.42 What reference spectra libraries are available in the toxicology section?

8 GAS CHROMATOGRAPHY QUANTITATION

8.1 Objectives

8.1.1 Become proficient in the operation of the various GCs used in the toxicology section.

8.1.2 Perform quantitative GC analyses of extracts from biological specimens for the presence of drugs.

8.1.3 Generate accurate and precise quantitative results.

8.1.4 Understand the use of internal and external standards, and quality control as applied to GC.

8.1.5 Construct and apply calibration curves using gas chromatography software.

8.1.6 Understand and explain the criteria for acceptance of quantitative data.

8.1.7 Demonstrate a working knowledge of reporting quantitative results in the manner used in the toxicology section

8.2 Estimated Time

One month

8.3 Methods of Instruction

8.3.1 Lectures

8.3.1.1 Result interpretation

8.3.1.2 Preparing a calibration curve

8.3.1.3 GC quantitative software

8.3.2 Required Reading

8.3.2.1 Barry Levine (2003) *Principles of Forensic Toxicology*, pp 89-116.

8.3.2.2 Toxicology Procedures Manual.

8.3.3 Demonstration

8.3.3.1 Use of gas chromatographs for quantiation will be observed from beginning to end and notes will be taken by the Trainee.

8.3.4 Laboratory Exercises

8.3.4.1 Spike, extract and analyze a basic drug mix calibration curve in blood. Extract and analyze quality control samples. Prepare a 1:1 and 1:2 dilution of the highest concentration quality control. Use GC software to create a calibration curve and determine quality control values. Determine LOD spike, LOQ and ULOQ for each drug in the mix.

8.3.4.2 Spike, extract and analyze an acid mix calibration curve in blood. Extract and analyze quality control samples. Prepare a 1:1 and 1:2 dilution of the highest concentration quality control. Use GC software to create a calibration curve and determine quality control values. Determine LOD spike, LOQ and ULOQ for each drug in the mix.

8.3.4.3 Spike, extract and analyze a carisoprodol and meprobamate calibration curve in blood. Extract and analyze quality control samples. Prepare a 1:1 and 1:2 dilution of the highest quality control. Use GC software to create a calibration curve and determine quality control values. Determine LOD spike, LOQ and ULOQ for each drug in the mix.

8.4 Evaluation

8.4.1 Completion of written study questions.

8.4.2 Laboratory Competency Testing

8.4.2.1 Perform a basic drug quantitation on at least 5 previously analyzed case samples. Include at least two different basic drugs. Acceptable performance is ± 20% of the reported quantitation.

8.4.2.2 Perform an acid drug quantitation on at least 3 previously analyzed case samples. Acceptable performance is ± 20% of the reported quantitation.

8.4.2.3 Perform a carisoprodol/meprobamate quantitation on at least 5 previously analyzed case samples. Acceptable performance is ± 20% of the reported quantitation.

8.4.3 Oral presentation followed by technical question/answer session.

8.5 Study Questions

8.5.1 Explain LOD, LOD spike, LOQ, ULOQ as applied to GC quantitative measurements.

8.5.2 Explain the SOP criteria concerning rejecting calibrator concentrations in a calibration curve.

8.5.3 Explain the reporting procedure for dilutions above and below the linear range of the calibration curve.

9 HPLC

9.1 Objectives

9.1.1 Understand the theory of high performance liquid chromatography (HPLC).

9.1.2 Become familiar with the practical aspects of HPLC.

9.1.3 Study the components of an HPLC and understand their function and specifics of operation.

9.1.4 Become proficient in the operation of the HPLC used in the toxicology section.

9.1.5 Perform quantitative HPLC analyses of extracts from biological specimens for the presence of drugs.

9.1.6 Examine and interpret chromatographic printouts.

9.1.7 Understand the use of internal and external standards, and quality control as applied to HPLC systems.

9.2 Estimated Time

Two months

9.3 Methods of Instruction

9.3.1 Lectures

9.3.1.1 Principles of HPLC

9.3.1.2 Parameters affecting the separation process and resolution of peaks

9.3.1.3 Components and operation of an HPLC

9.3.1.4 Types of columns

9.3.1.5 Types of detectors

9.3.1.6 HPLC optimization

9.3.1.7 Result interpretation

9.3.2 Required Reading

9.3.2.1 M Moffat, A.C., editor. *Clarke's Analysis of Drugs and Poisons,* 3rd edition. London: The Pharmaceutical Press, 2004 pp 500-534.

9.3.2.2 *Forensic Applications of High-Performance Liquid Chromatography and Capillary Electrophoresis* in Saferstein's *Forensic Science Handbook*. Englewood Cliffs, NJ: Prentice Hall, 1982 pp 1-27.

9.3.2.3 Toxicology Procedures Manual.

9.3.3 References

9.3.3.1 R Willoughby, E Sheehan, S Mitrovich. *A Global View of LC/MS: How to Solve your Most Challenging Analytical Problems*. Pittsburgh, PA: Global View Publishing, 1998.

9.3.4 Demonstration

9.3.4.1 Use of an HPLC will be observed from beginning to end and notes will be taken by the Trainee.

9.3.5 Laboratory Exercises

9.3.5.1 Run benzodiazepine calibrators A, B and C on HPLC. Identify each benzodiazepine by retention time and UV spectral library matching.

9.3.5.2 Run acetaminophen and salicylate calibrators. Identify each by retention time and UV spectral library matching.

9.4 Evaluation

9.4.1 Completion of written study questions.

9.4.2 Laboratory Competency Testing

9.4.2.1 Perform a quantitative benzodiazepine analysis of 10 unknown samples. The batch should include instrument preparation (buffers, backflush, prime etc.), calibrators, controls and case samples. Identify each benzodiazepine by retention time and UV spectral library matching.

9.4.2.2 Alternatively, an analogous acetaminophen/salicylate batch may be substituted as directed by the Training Coordinator.

9.4.3 Oral presentation followed by technical question/answer session.

9.5 Study Questions

9.5.1 Compare and contrast gas chromatography and liquid chromatography.

9.5.2 What are some of the advantages of liquid chromatography?

9.5.3 Draw a schematic diagram of a HPLC system and describe the function of each component.

9.5.4 Define the following:

- Mobile phase
- Capacity factor
- Isocratic elution
- Gradient elution
- Normal phase HPLC
- Ion chromatography
- Reverse phase HPLC
- HILIC

9.5.5 Describe the photodiode array detector. What are the advantages of diode array detection? What other detectors are available for HPLC systems?

9.5.6 Describe UV spectral library matching. What criteria are required to establish a match?

9.5.7 Describe some of the techniques used to interface the HPLC with a mass spectrometer.

9.5.8 Describe the use of buffers giving examples and their use for specific separations. How do buffers differ between HPLC and LCMS analyses?

9.5.9 Two peaks co-elute. What changes to mobile phase might help improve the resolution? What changes to stationary phase might help improve the resolution?

9.5.10 Describe the HPLC columns used in the toxicology laboratory. What are the advantages of each?

9.5.11 Describe the effect of particle size on separation with HPLC columns.

10 MASS SPECTROMETRY QUANTITATION

10.1 Objectives

10.1.1 Become proficient in the utilization of GCMS in the selected ion monitoring mode.

10.1.2 Generate and evaluate mass spectral information to quantitate the drugs being analyzed.

10.1.3 Perform routine maintenance on the mass spectrophotometer.

10.1.4 Perform quantitative GCMS analyses of extracts from biological specimens for the presence of drugs.

10.1.5 Generate accurate and precise quantitative results.

10.1.6 Understand the use of deuterated internal standards, and quality control as applied to GCMS.

10.1.7 Perform derivatized drug quantitations. Understand the role of derivatization.

10.1.8 Construct and apply calibration curves using GCMS software.

10.1.9 Understand and explain the criteria for acceptance of quantitative GCMS data.

10.1.10 Demonstrate a working knowledge of reporting quantitative GCMS results in the manner used in the toxicology section.

10.2 Estimated Time

Two months, part time

10.3 Methods of Instruction

10.3.1 Lecture

10.3.1.1 Selected Ion Mode (SIM) of operation

10.3.1.2 Specimen preparation (dilution, internal standard, derivatization)

10.3.1.3 Spectral interpretation

10.3.1.4 Use of GCMS software to generate a calibration curve for SIM data

10.3.1.5 Derivatized extractions

10.3.2 Required Reading

10.3.2.1 McLafferty, F. W., *Interpretation of Mass Spectra*, 3Ed. Chap 1.

10.3.2.2 Moffat, A. C., editor. *Clarke's Analysis of Drugs and Poisons*, 3rd Ed. The Pharmaceutical Press, London, 2004. pp 379-391.

10.3.2.3 Toxicology Procedures Manual

10.3.2.4 Barry Levine (2003) *Principles of Forensic Toxicology*, pp 139-153.

10.3.3 Demonstration

10.3.3.1 Extraction and derivatization of a drug in biological specimens with GCMS SIM quantitation will be observed from beginning to end and notes will be taken by the Trainee.

10.3.4 Laboratory Exercises

10.3.4.1 Perform an SPE opiate quantitation of calibrators and controls.

10.3.4.2 Perform a liquid–liquid amphetamine quantitation of calibrators and controls.

10.3.4.3 Perform a GCMS SIM barbiturate quantitation of calibrators and controls.

10.3.4.4 Perform daily routine maintenance of the GC/MS to include but not limited to changing or adjusting the autotune, liner, septum, seals, gap column, transfer lines, gold seal, etc.

10.4 Evaluation

10.4.1 Completion of written study questions.

10.4.2 Laboratory Competency Testing

10.4.2.1 Perform a cocaine quantitation on at least 5 previously analyzed case samples. Acceptable performance is ± 20% of the reported quantitation.

10.4.2.2 Perform an opiate quantitation on at least 5 previously analyzed case samples. Acceptable performance is ± 20% of the reported quantitation.

10.4.2.3 Perform an amphetamine quantitation on at least 3 previously analyzed case samples. Acceptable performance is ± 20% of the reported quantitation.

10.4.3 Oral presentation followed by technical question/answer session.

10.5 Study Questions

10.5.1 Explain LOD spike, LOD, LOQ, ULOQ as applied to GCMS quantitative measurements.

10.5.2 Define and explain the following:

- Blank and negative control
- Internal standard
- External standard
- Positive Control
- Calibrator

10.5.3 Describe silylation, methylation, and acylation.

10.5.4 Describe and/or draw the derivative formed using the Toxicology Procedures Manual for morphine, benzoylecgonine, butalbital, amphetamine and tetrahydrocannabinol (GC/MS).

10.5.5 How would the following be reported?

10.5.5.1 Drug concentration is greater than the ULOQ.

10.5.5.2 Drug concentration is below LOQ but above LOD spike and has acceptable ion ratios.

10.5.5.3 Drug concentration is below LOQ but above LOD spike and one ion ratio is unacceptable.

10.5.5.4 Drug concentration is below LOQ and LOD spike with one ion ratio unacceptable.

11 TANDEM MASS SPECTROMETRY (LCMSMS)

11.1 Objectives

11.1.1 Understand and explain the operation of LC-MS interface.

11.1.2 Understand and explain ion formation.

11.1.3 Understand and explain tandem mass spectrometry.

11.1.4 Perform routine maintenance and tuning of the LCMSMS.

11.1.5 Generate and evaluate mass spectral information to confirm and quantitate the drugs being analyzed.

11.1.6 Construct and apply calibration curves using LCMSMS software.

11.1.7 Understand and explain the criteria for acceptance of quantitative LCMSMS data.

11.1.8 Demonstrate a working knowledge of reporting quantitative LCMSMS results in the manner used in the toxicology section

11.2 Estimated Time

Two months

11.3 Methods of Instruction

11.3.1 Self-Directed Study

11.3.1.1 Principles of tandem mass spectrometry.

- Ion Sources: ESI, APCI
- Ion Focusing Optics/Lenses
- QQQ: quadrupoles, collision cells

11.3.1.2 Modes of operation: MS1/MS2 Scan, SRM, MRM, Product Ion Scan, Precursor Ion Scan

11.3.1.3 MS components (sample inlets, focusing components, quadrupoles, collision cell, HED)

11.3.1.4 Optimization of targets: purpose, parameters

11.3.1.5 Principles of method development and validation

11.3.1.6 Acquisition of data

11.3.1.7 Qualitative results

11.3.1.8 Quantitative Analysis: overview, data interpretation, batch report generation

11.3.2 Literature Reading

11.3.2.1 Virginia DFS Toxicology Procedures Manual

11.3.2.2 Agilent Technologies 6400 Series QQQ LC/MS Techniques and Operation – Student Manual, pp. 12-28, 35-65, 93-112, 148-168, 300-320.

11.3.2.3 Agilent Technologies 6400 Series Triple Quad LC/MS System Manuals

- Concepts Guide – Ch. 2-3
- Maintenance Guide – pp. 8-22, 67-72, 103-112
- Optimizer Technical Overview

11.3.2.4 Agilent Technologies LC-MSD Maintenance Videos – www.chem.agilent.com/en-US/Products/Instruments/lc/1100series/Pages/lc-msd.aspx

11.3.3 Demonstration

11.3.3.1 Observe extraction of a drug from a biological specimen and analysis by LCMSMS. LCMSMS operation and use of quantitative software will be observed from beginning to end and notes will be taken by the Trainee.

11.3.4 Laboratory Exercises

11.3.4.1 Perform daily and weekly maintenance procedures. This is to include the evaluation of a Checktune, cleaning of the ion source, and the preparation of fresh solvents.

11.3.4.2 Review the results of an Autotune report. Evaluate the report.

11.3.4.3 Using Quantitative Analysis, generate and process a set of previously acquired data.

11.3.4.4 Spike, extract and analyze a benzodiazepine calibrator mix curve in blood. Extract and analyze quality control samples. Use LCMSMS software to create a calibration curve and determine quality control values. Determine LOD spike, LOQ and ULOQ for each drug in the mix.

11.3.4.5 Spike, extract and analyze THC and THCA calibrators curve in blood. Extract and analyze quality control samples. Use LCMSMS software to create a calibration curve and determine quality control values. Determine LOD spike, LOQ and ULOQ for each drug in the mix.

11.4 Evaluation

11.4.1 Completion of written study questions.

11.4.2 Laboratory Competency Testing

11.4.2.1 Perform a benzodiazepine quantitation on at least 10 previously analyzed case samples. Acceptable performance is ± 20% of the reported quantitation.

11.4.2.2 Perform a THC/THCA quantitation on at least 10 previously analyzed case samples. Acceptable performance is ± 20% of the reported quantitation

11.4.3 Oral presentation followed by technical question/answer session.

11.5 Study Questions

11.5.1 Discuss the advantages and disadvantages of the following comparisons:

- LC/MS vs. LC/MS-MS
- GC-EI-MS vs. LC/MS-MS

11.5.2 Draw a schematic diagram for LC/MS-MS. Label and describe the functions of each component.

11.5.3 Discuss the use of various buffers and acid additives within the mobile phase with respect to LC/MS-MS.

11.5.4 Define the term transition and relate it to GC/MS SIM analysis. Explain how each provide appropriate specificity and quanitative information for the two types of anlyses.

11.5.5 Diagram an electrospray ionization source (can utilize schematic from 11.5.2).

11.5.5.1 Explain the ionization process.

11.5.5.2 What is coulombic explosion?

11.5.5.3 What is the purpose of the drying gas?

11.5.6 What vacuum conditions are necessary in LC/MS-MS?

11.5.7 Discuss ion suppression and how it can affect LC/MS-MS analysis.

11.5.8 Explain the following with examples from the Agilent 6400 Series LC/MS-MS. When does the operator perform each of these activities?

- Check-tune
- Auto-tune

12 COURTROOM TESTIMONY

12.1 Objectives

12.1.1 To familiarize the trainee with the functions of a criminal courtroom proceeding

12.1.2 To have the trainee prepare a current curriculum vitae (or resume) and properly answer *voir dire* questioning

12.1.3 To familiarize the trainee with proper methods of presenting expert testimony

12.2 Estimated Time

One month

12.3 Methods of Instruction

12.3.1 Reading assignments

12.3.2 Observation of expert testimony

12.3.3 Answering study questions throughout training modules to lay jury or judge

12.3.4 Practical exercises (mini-moot courts)

12.3.5 Required Reading

12.3.5.1 Kuzmack, N.T., JD, MA. *Legal Aspects of Forensic Science* in Saferstein's *Forensic Science Handbook*. Englewood Cliffs, NJ: Prentice Hall, 1982 pp 1-27.

12.3.5.2 Babitsky S. and J. Mangraviti. *How to Excel during Cross-Examination. Techniques for Experts that Work.* Falmouth, MA: SEAK, 1997.

12.3.5.3 Kogan, J. *Being a Good Expert Witness in a Criminal Case*. J For Sci 23(1): 190-200, 1978.

12.3.5.4 Kates, James H. and Henry K. Guttenplan, Ph.D. *Ethical Considerations in Forensic Science Services* J For Sci 28(4): 972-976, 1983.

12.3.5.5 Keefe, J.F. *Forensic Sciences: Criminal Justice System Viewed by the Defense.* 12(2):59, 1980.

12.3.5.6 Lucas, Douglas M., M.Sc. *The Ethical Responsibilities of the Forensic Scientist: Exploring the Limits* J For Sci 34(3):719-729, 1989.

12.3.5.7 Saks, Michael J., Ph.D., M.S.L. *Prevalence and Impact of Ethical Problems in Forensic Science* J For Sci 34(3): 772-793, 1989.

12.3.5.8 Schroeder, Oliver C., J.D. *Ethical and Moral Dilemmas Confronting Forensic Scientists* J For Sci 29(4): 966-986, 1984.

12.3.5.9 Wu, A., Hill, D., Crouch, D., Hodnett, N., and H. McCurdy. *Minimal Standards for the Performance and Interpretation of Toxicology Tests in Legal Proceedings.* J For Sci 44(3): 516-522, 1999.

12.3.5.10 Saady, J. *Ethics for Toxicologists: An Examination of Conscience* J Anal Tox 25:390 - 392, 2001.

12.3.6 Demonstration

12.3.6.1 The trainee will observe at least 5-10 expert courtroom testimonies. Discuss testimony with each examiner. Document each observed testimony with name of examiner, date, court and notes reflecting the testimony and discussion.

12.3.7 Practical Exercises

12.3.7.1 Complete required reading assignments

12.3.7.2 Complete curriculum vitae or resume

12.3.7.3 Mini moot courts

12.4 Evaluation

12.4.1 Completion of written study questions.

12.4.2 Courtroom Exercise

12.4.2.1 The Trainee must be capable of answering questions on this Module such as would be expected in a courtroom scenario.

12.5 Study Questions

12.5.1 Discuss the role of the following during a trial:

12.5.1.1 Expert witness

12.5.1.2 Judge

12.5.1.3 Prosecutor

12.5.1.4 Defendant

12.5.1.5 Defense counsel

12.5.1.6 Jury

12.5.2 Define the following:

12.5.2.1 Voir dire

12.5.2.2 Direct examination

12.5.2.3 Cross examination

12.5.2.4 Redirect

12.5.2.5 Chain of custody

12.5.3 Define the word *ethics*.

12.5.3.1 Why is it important in forensic science?

12.5.3.2 Investigate and describe the Code of Ethics for DFS, AAFS, ASCLD/LAB, SOFT and ABFT.

12.5.3.3 Give some examples of ethical violations and sanctions imposed by forensic organizations.

12.5.4 Verbally answer the following questions to the training coordinator or designee:

12.5.4.1 What is your name?

12.5.4.2 What is your occupation?

12.5.4.3 For whom do you work?

12.5.4.4 How long have you been so employed?

12.5.4.5 What are your duties in this occupation?

12.5.4.6 What education and training do you possess that qualifies you to perform your duties?

12.5.4.7 What specific courses have you taken that are directly related to toxicology analysis?

12.5.4.8 How are these courses related? For example, what did you learn in your general chemistry course that aids you in the analysis of forensic toxicology samples?

12.5.4.9 What is the definition of an expert witness?

12.5.4.10 Is the university/college you graduated from accredited, and if so, by whom?

12.5.4.11 Who conducted your training?

12.5.4.12 What are his/her/their qualifications?

12.5.4.13 What literature do you read relating to your job?

12.5.4.14 How many analyses have you done on forensic cases?

12.5.4.15 Do you belong to a recognized society attesting to your qualifications in toxicology?

12.5.4.16 Have you written any articles or published materials dealing with your work?

13 ALCOHOLIC BEVERAGE ANALYSIS

13.1 Objectives

13.1.1 Display a working knowledge of alcoholic beverages (history, terminology, manufacturing processes, chemical formulations and compositions of various beverages).

13.1.2 Demonstrate proficiency in the analysis of beverages for alcohol content.

13.2 Estimated Time

Two months

13.3 Methods of Instruction

13.3.1 Lectures

13.3.1.1 Manufacturing of alcoholic beverages

13.3.1.2 Physical make up of alcoholic beverages

13.3.1.3 Chemical formulations and compositions of alcoholic beverages

13.3.1.4 Principles of direct injection GC

13.3.2 Literature Review

13.3.2.1 Amerine, M. *Laboratory Procedures for Enologists.* UC Davis, 1967.

13.3.2.2 Barnett, J.H. and J.R. Einsman. *Occurrence and Distribution of Congeners in Distilled Alcohol Spirits*. J Assoc of Official Analytical Chemists Vol 60, 1977.

13.3.2.3 Lange, N.A. *Lange's Handbook of Chemistry*. New York: McGraw-Hill, 1967.

13.3.2.4 Lembeck, H. *Grossman's Guide to Wine, Beers and Spirits.* New York: Charles Scribner's Sons, 1983.

13.3.2.5 Lichine, A. *Alexis Lichine's Encyclopedia of Wines and Spirits*. New York: Alfred Knopf, Inc., 1983.

13.3.2.6 *Official Methods of Analysis of the Association of Official Analytical Chemists*. 15th Ed., 1990.

13.3.2.7 Slavin, M. *Atomic Absorption Spectroscopy*. New York: John Wiley and Sons, Inc., 1978.

13.3.3 Demonstration

13.3.3.1 Alcoholic beverage analyses will be observed from beginning to end and notes will be taken by the Trainee.

13.3.4 Laboratory Exercises

13.3.4.1 Perform ethanol content analyses on 20 different alcoholic beverages

13.4 Evaluation

13.4.1 Completion of written study questions.

13.4.2 Laboratory Competency Testing

13.4.2.1 A series of at least 20 different alcoholic beverages will be presented to the Trainee for a routine alcohol content determination. Quantitative results must agree within ± 10 % of the previous results.

13.4.3 Oral presentation followed by technical question/answer session.

13.5 Study Questions

13.5.1 Explain when calibration or recalibration of the headspace GC is necessary. How is recalibration accomplished?

13.5.2 What is NIST? Why is it important?

13.5.3 Describe the ranges of alcohol content for the following alcoholic beverages: table wines, fortified wines, light beer, premium beer, malt liquors, special stouts, and distilled spirits.

13.5.4 What are ethanolic congeners?

13.5.5 What is proof?

13.5.6 What is fermentation?

13.5.7 What is mash?

13.5.8 What is distillation?

13.5.9 What are distilled spirits?

13.5.10 Describe any differences between the Blood Alcohol method and the ABC Alcohol method.

14 PHARMACOLOGY AND TOXICOLOGY

14.1 Objectives

14.1.1 Display a working knowledge of the various categories of drugs encountered in toxicological analysis.

14.1.2 Understand the differences in interpretation for medical examiner (ME) cases vs. driving under the influence of drug (DUID) cases. Explain how the same drug concentration may be interpreted differently.

14.1.3 Know and understand the pharmacodynamic and pharmacokinetic properties of major drug classes.

14.1.4 Understand how the therapeutic, toxic and lethal blood concentrations are assigned and used for populations, but may vary for an individual.

14.1.5 Explain the pharmacodynamic effects on human behavior and performance using blood drug concentrations as it pertains to court testimony and DUID cases.

14.1.6 Understand the process of postmortem redistribution, the interpretation of cases where this occurs, and which drugs are expected to undergo this process.

14.2 Estimated Time

Four months

14.3 Methods of Instruction

14.3.1 Lectures

14.3.1.1 SOFT Forensic Toxicology Review Course Lectures 2003

14.3.1.2 Specific lecture topics for each class of drugs

14.3.1.2.1 General pharmacokinetic parameters (Vd, t ½ ,metabolism)

14.3.1.2.2 Major therapeutic and/or illicit uses

14.3.1.2.3 Therapeutic effects

14.3.1.2.4 Side effects

14.3.1.2.5 Effects on driving

14.3.1.2.6 Concentrations at which effects are observed

14.3.1.2.7 Comparison of concentrations in DUID vs postmortem cases

14.3.1.2.8 Potential drug interactions

14.3.1.2.9 Postmortem redistribution

14.3.1.2.10 Practice trial testimony

14.3.2 Literature Review

14.3.2.1 Barry Levine (2003) *Principles of Forensic Toxicology*.

14.3.2.2 Goodman and Gilman (1996) *The Pharmacologic Basis of Therapeutics*.

14.3.2.3 Garriott (2003*) Medicolegal Aspects of Alcohol.*

14.3.2.4 SOFT Forensic Toxicology Review Course, Raleigh Durham, NC, 2003.

14.3.2.5 *National Highway Safety Traffic Administration, Drugs and Human Performance Fact Sheets*, 2004.

14.3.2.6 *The Effects of Drugs on Human Performance and Behavior*, Forensic Science Review 14: Jan 2002.

14.3.3 Discussion of interpretation and testimony.

14.3.4 Practice testimony on each drug class (mini moot courts).

14.4 Evaluation

14.4.1 Written study questions on each class or drugs.

14.4.2 Mini mock trials on each class of drugs

14.4.2.1 The Trainee must be capable of answering questions on each class of drugs such as would be expected in courtroom scenario.

14.5 Pharmacodynamics and Pharmacokinetics including Neurotransmission, Drug-Receptor Interactions, and Dose/Response

14.5.1 Additional Lectures

14.5.1.1 SOFT Pharmacokinetics Workshop 2006

14.5.2 Required Literature Reading

14.5.2.1 Levine Principles of Forensic Toxicology, Ch 4

14.5.2.2 Goodman and Gilman The Pharmacologic Basis of Therapeutics, Ch 1-4, 12

14.5.3 Study questions

14.5.3.1 Define pharmacokinetics.

14.5.3.2 Define pharmacodynamics.

14.5.3.3 What factors influence absorption?

14.5.3.4 Will a weak base be absorbed primarily in stomach or small intestine? Why? What about a weak acid?

14.5.3.5 Define bioavailability.

14.5.3.6 What is Vd? How is it calculated?

14.5.3.7 Describe zero and first order elimination. Diagram each.

14.5.3.8 Define first pass effect.

14.5.3.9 Give 5 examples of different routes of administration and a drug example for each. Describe how each route of administration would affect onset of action and peak blood concentration.

14.5.3.10 Give two examples of phase I and phase II reactions. Give a drug example for each.

14.5.3.11 Diagram a dose/response curve. What would be the effect of adding an antagonist? Adding a non-competitive antagonist?

14.5.3.12 Diagram a neuronal synapse. Describe how reuptake inhibitors influence this environment.

14.5.3.13 What is therapeutic index? How is it calculated? Give an example of a drug with a high therapeutic index. Give an example of a drug with a low therapeutic index.

14.6 Alcohol Pharmacology, Impairment and Courtroom Testimony

14.6.1 Required Literature Reading

14.6.1.1 Levine *Principles of Forensic Toxicology*, Ch 10.

14.6.1.2 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 18.

14.6.1.3 Garriott *Medicolegal Aspects of Alcohol*, Ch 2-4 (pharmacology), 13-15 (impairment), 17-19 (testimony).

14.6.2 Study questions

14.6.2.1 Mr. Jones got in an accident at 0015 hrs. He admitted to drinking 3 beers rapidly at 1130hrs. His blood was drawn at 0200 hrs and the result was 0.20 % w/v. What would his blood alcohol concentration been at the time of the accident?

14.6.2.2 How many beers would Mr. Jones have to consume to reach 0.20% BAC?

14.6.2.3 Describe the effects of alcohol on driving.

14.6.2.4 What blood ethanol concentrations could result from postmortem changes?

14.6.2.5 Approximately how long would it take someone with a BAC of 0.30 %w/v to metabolize all the alcohol in the body?

14.7 Opioids (Natural, Synthetic and Semisynthetic)

14.7.1 Required Literature Reading

14.7.1.1 Levine *Principles of Forensic Toxicology*, Ch 12.

14.7.1.2 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 23-24.

14.7.1.3 NHTSA: Methadone, morphine

14.7.2 Study questions

14.7.2.1 Differentiate between the terms opiate, opioid and narcotics.

14.7.2.2 Discuss the structure-activity relationship of morphine and its opiate analogs versus the opiate antagonist, naloxone.

14.7.2.3 Which of the following are used to synthesize opioids? Give specific products.

14.7.2.3.1 Morphine

14.7.2.3.2 Codeine

14.7.2.3.3 Papaverine

14.7.2.3.4 Noscopine

14.7.2.3.5 Thebaine

14.7.2.4 Discuss absorption, distribution, metabolism and elimination (ADME) of heroin.

14.7.2.5 Discuss the role of codeine and 6MAM in the determination of whether a death involved heroin.

14.7.2.6 What is the classical clinical presentation of acute opiate toxicity?

14.7.2.7 Discuss the pharmacologic CNS effects of opiates that would be relevant in a DUID case.

14.8 Cocaine/Benzoylecgonine

14.8.1 Required Literature Reading

14.8.1.1 Levine *Principles of Forensic Toxicology*, Ch 13.

14.8.1.2 NHTSA: Cocaine

14.8.1.3 FSR: Cocaine

14.8.2 Study questions

14.8.2.1 What is CBN?

14.8.2.2 What are the effects of cocaine on catecholamines?

14.8.2.3 What is neurotransmitter depletion? How is it related to cocaine use?

14.8.2.4 What are the effects of cocaine on drivers at the following concentrations?

14.8.2.4.1 Cocaine 0.02 mg/L, benzoylecgonine 0.3 mg/L

14.8.2.4.2 Cocaine ND, benzoylecgonine 2.0 mg/L

14.9 Cannabinoids

14.9.1 Required Literature Reading

14.9.1.1 Levine *Principles of Forensic Toxicology*, Ch 14.

14.9.1.2 FSR: Cannabinoids

14.9.1.3 NHTSA: Cannabinoids

14.9.2 Study questions

14.9.2.1 A Commonwealth Attorney calls to discuss the following cases. What would you say?

14.9.2.1.1 THC 0.001 mg/L, THCA 0.02 mg/L. Driver pulled over for bad driving, officer witnessed suspect throw joint out of window, failed all FSTs.

14.9.2.1.2 THC 0.001 mg/L, THCA 0.02 mg/L. Driver pulled over for broken tail light, defendant admitted to smoking a joint the night before, performed fairly well FSTs.

14.9.2.2 Is there an established relationship between THC blood concentration and driving impairment? Discuss why or why not.

14.9.2.3 What are the major metabolites of THC? Are they active/inactive? Which one does DFS analyze and why?

14.9.2.4 Describe ADME of THC.

14.9.2.5 THC has a broad spectrum of pharmacologic effects. Describe each. Can THC be classified in one drug category?

14.9.2.6 Describe the effects of THC on driving.

14.10 CNS Depressants (Benzodiazepines, Barbiturates, Carisoprodol, Zolpidem, GHB, etc.)

14.10.1 Required Literature Reading

14.10.1.1 Levine *Principles of Forensic Toxicology*, Ch 11.

14.10.1.2 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 17.

14.10.1.3 FSR: Benzodiazepines, GHB

14.10.1.4 NHTSA: Carisoprodol, GHB, zolpidem

14.10.2 Study questions

14.10.2.1 Make a table listing at least all CNS depressant drugs analyzed in DUID cases. Include:

14.10.2.1.1 Dosage form

14.10.2.1.2 Therapeutic uses

14.10.2.1.3 Therapeutic range

14.10.2.1.4 Toxic concentrations

14.10.2.1.5 Lethal concentrations

14.10.2.1.6 Half-life

14.10.2.1.7 Detection time in blood

14.10.2.1.8 Detection time in urine

14.10.2.1.9 Typical adverse side effects

14.11 Sympathomimetic Amines (Methamphetamine, Amphetamine, MDMA, Ephedrine, Methylphenidate)

14.11.1 Required Literature Reading

14.11.1.1 Levine *Principles of Forensic Toxicology*, Ch 15.

14.11.1.2 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 10.

14.11.1.3 FSR: Methamphetamine

14.11.1.4 NHTSA: Methamphetamine, MDMA

14.11.2 Study questions

14.11.2.1 What are the common neurotransmitters involved in sympathomimetic pathways?

14.11.2.2 What are the common structural properties of these neurotransmitters?

14.11.2.3 How does hydroxylation affect their action?

14.11.2.4 Compare ADME for methamphetamine and MDMA. Include concentrations that contribute to observed effects and discuss tolerance.

14.11.2.5 What "rave" accessory is used to provide protection from a common MDMA side effect?

14.11.2.6 PMA/PMMA are sometimes unknowingly substituted for MDMA. What adverse effects does this have on the unsuspecting "raver"?

14.11.2.7 Discuss the effects of methamphetamine and MDMA on driving.

14.11.2.8 Sympathomimetic amines are usually present in racemic mixtures. Describe the different properties of d and l methamphetamine and MDMA.

14.12 Hallucinogens (LSD, PCP, Ketamine, Psilocybin)

14.12.1 Required Literature Reading

14.12.1.1 Levine *Principles of Forensic Toxicology*, Ch 16.

14.12.1.2 FSR: Ketamine

14.12.1.3 NHTSA: Ketamine, LSD, PCP

14.12.2 Study questions

14.12.2.1 Which neurotransmitters are responsible for the hallucinogenic properties of compounds?

14.12.2.2 Compare ADME of LSD and PCP. Include dosage and detection times.

14.12.2.3 Discuss significant adverse effects of hallucinogenic drugs on driving.

14.12.2.4 What are the lethal toxic effects of hallucinogenic drugs?

14.12.2.5 What is the prevalence of hallucinogenic drug use in the general population?

14.13 Neuroleptics (Antipsychotics)

14.13.1 Required Literature Reading

14.13.1.1 Levine *Principles of Forensic Toxicology*, Ch 19.

14.13.1.2 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 18.

14.13.2 Study questions

14.13.2.1 Give 2 examples each of old and new generation neuroleptics.

14.13.2.2 Describe ADME for each.

14.13.2.3 What are some of the side effects of old and new generation neuroleptics?

14.13.2.4 What are some of the advantages of the new generation neuroleptics?

14.14 Antidepressants (MAO, TCA, SSRI)

14.14.1 Required Literature Reading

14.14.1.1 Levine *Principles of Forensic Toxicology*, Ch 18.

14.14.1.2 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 19.

14.14.2 Study questions

14.14.2.1 What are some of the side effects that would result from tricyclic antidepressant combined concentrations of 0.1 mg/L amitriptyline and 0.5 mg/L nortriptyline?

14.14.2.2 Compare and contrast mechanisms of action, ADME and side effects of TCAs, SSRIs and MAOs.

14.15 Anticonvulsants (Phenytoin, Carbamazepine, Valproic acid, Gabapentin, Lamotrigine, Topiramate)

14.15.1 Required Literature Reading

14.15.1.1 Levine *Principles of Forensic Toxicology*, Ch 17.

14.15.1.2 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 21.

14.15.2 Study questions

14.15.2.1 Drugs used to control seizures have varied chemical structures. Describe each.

14.15.2.2 Describe the neurological pathways of seizure control.

14.15.2.3 Describe lethal toxicities associated with seizure medications.

14.15.2.4 Describe the metabolism of carbamazepine and its significance.

14.15.2.5 Describe the adverse effects of seizure medication on driving.

14.15.2.6 In OCME cases, what is the most important reason for the analysis of seizure medications?

14.16 Antihistamines/NSAIDS (Diphenhydramine, Promethazine, Dextromethorphan, ASA, APAP)

14.16.1 Required Literature Reading

14.16.1.1 Goodman and Gilman *The Pharmacologic Basis of Therapeutics*, Ch 25, 27

14.16.1.2 NHTSA: Diphenhydramine, dextromethorphan

14.16.2 Study questions

14.16.2.1 Make a table of histamine receptors including localization within the body, antagonists associated with each and the therapeutic uses, therapeutic/toxic levels, therapeutic effects and effects on driving for each antagonist.

14.16.2.2 Why do antihistamines have anticholinergic effects?

14.16.2.3 Describe postmortem redistribution of antihistamines.

14.16.2.4 What antihistamines are used in a DFSA? What screening method is used to detect them? What is their detection time in blood and urine?

15 DATA REVIEW AND CASE EXAMINATION

15.1 Objectives

15.1.1 To learn the process and documentation involved in data review.

15.1.2 To learn the process and documentation involved in case examination.

15.1.3 To learn the process for creating and releasing cases using LIMS.

15.2 Estimated Time

Two months

15.3 Methods of Instruction

15.3.1 Data review and case examination training is primarily learned by observing multiple certified examiners and performing training examinations that are critiqued by certified examiners

15.3.2 Trainee will observe and take notes of data review process with at least two experienced data reviewers.

15.3.3 Trainee will observe and take notes of case examination process with at least two experienced examiners.

15.3.4 Trainee will observe and take notes on LIMS Certificate of Analysis creation, technical review and release with at least two experienced examiners.

15.3.5 Trainee will review the Toxicology Procedures Manual.

15.4 Laboratory Exercises

15.4.1 Perform data review on alcohol, immunoassay, drug screen, GC quantitation, GCMS quantitation, LCMSMS quantitation batches with at least two different examiners.

15.4.2 Perform case examinations on 10 non-implied consent cases with at least two different examiners (total 20 cases minimum). Cases must be a variety and include homicide, drug overdose, sexual assault (at least one), positive ethanol/drugs manslaughter, and decomposition cases (at least two). Medical examiner ethanol only cases are not included.

15.4.3 Perform 10 DUID/DUI case examinations with at least two different toxicologists/examiners (total 20 cases minimum). No more than 5 ethanol only cases and 2 negative tox cases can be included in the 20.

15.5 Evaluation

15.5.1 Non-Implied Consent cases. Trainer will select 20 cases that have not had final case examination performed. Trainee will perform final case examination using a Toxicology Summary Worksheet marked as a training case and submit cases to trainer for evaluation.

15.5.2 DUID/DUI cases. Trainer will select 20 DUID/DUI cases that have not had final case examination performed. Trainee will perform final case examination using a Toxicology Summary Worksheet marked as a training case and submit cases to trainer for evaluation. Alternately, the data from released cases may be used.

15.6 Study Questions

15.6.1 What does the analyst date on the batch chain-of-custody indicate?

15.6.2 How many controls must be acceptable in a drug quantitative batch?

15.6.3 How is carryover monitored in a drug quantitation?

15.6.4 Describe occasions when a drug may be reported as present.

15.6.5 An OCME case history lists rule out heroin. The blood morphine quantitation is 0.10 mg/L, 6AM none detected. As final case examiner, is this case complete? What other questions might you consider?

15.6.6 A methadone quantitation was performed on femoral blood and heart blood. Would you expect the methadone concentrations to be different and if so why?

15.6.7 A sexual assault case has immunoassay blood benzodiazepine negative, urine benzodiazepine pending and benzodiazepine quantitation none detected. As final case examiner is benzodiazepine testing complete?

15.6.8 Hospital blood and urine are submitted in a DUI manslaughter case. The blood alcohol was 0.10% on two separate aliquots. Would you order a urine alcohol and why or why not?

APPENDIX A

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